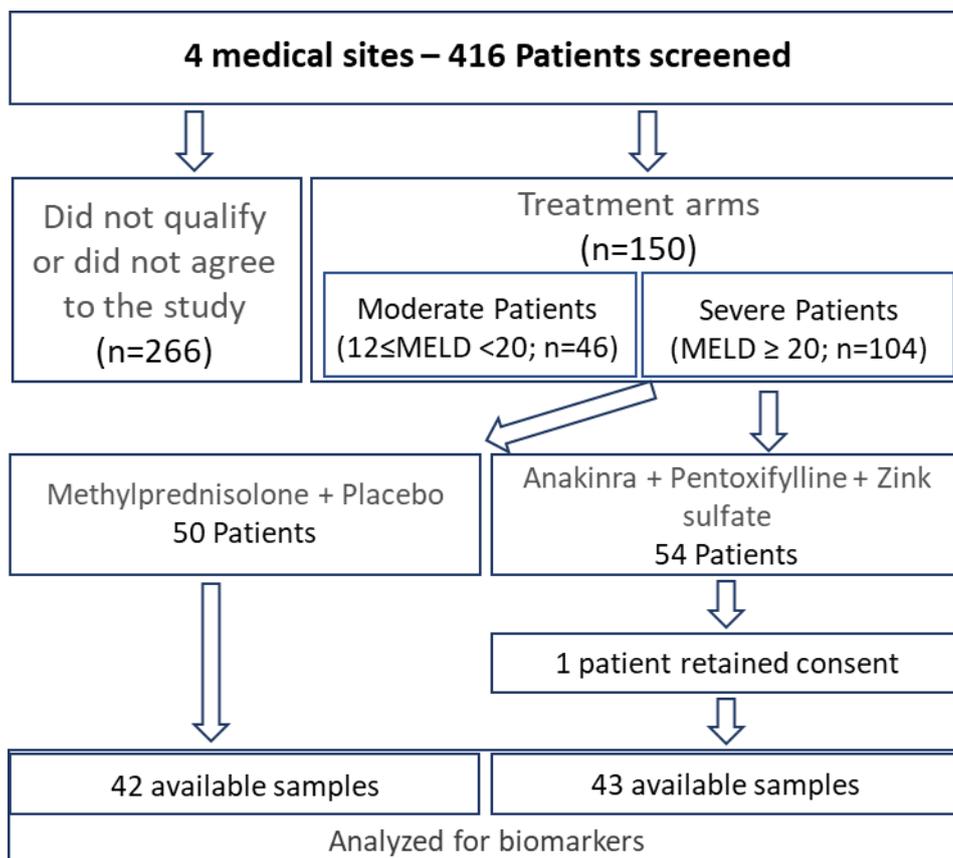


A novel score of IL-13 and age predicts 90-day mortality in severe alcohol-associated hepatitis – a multicenter plasma biomarker analysis

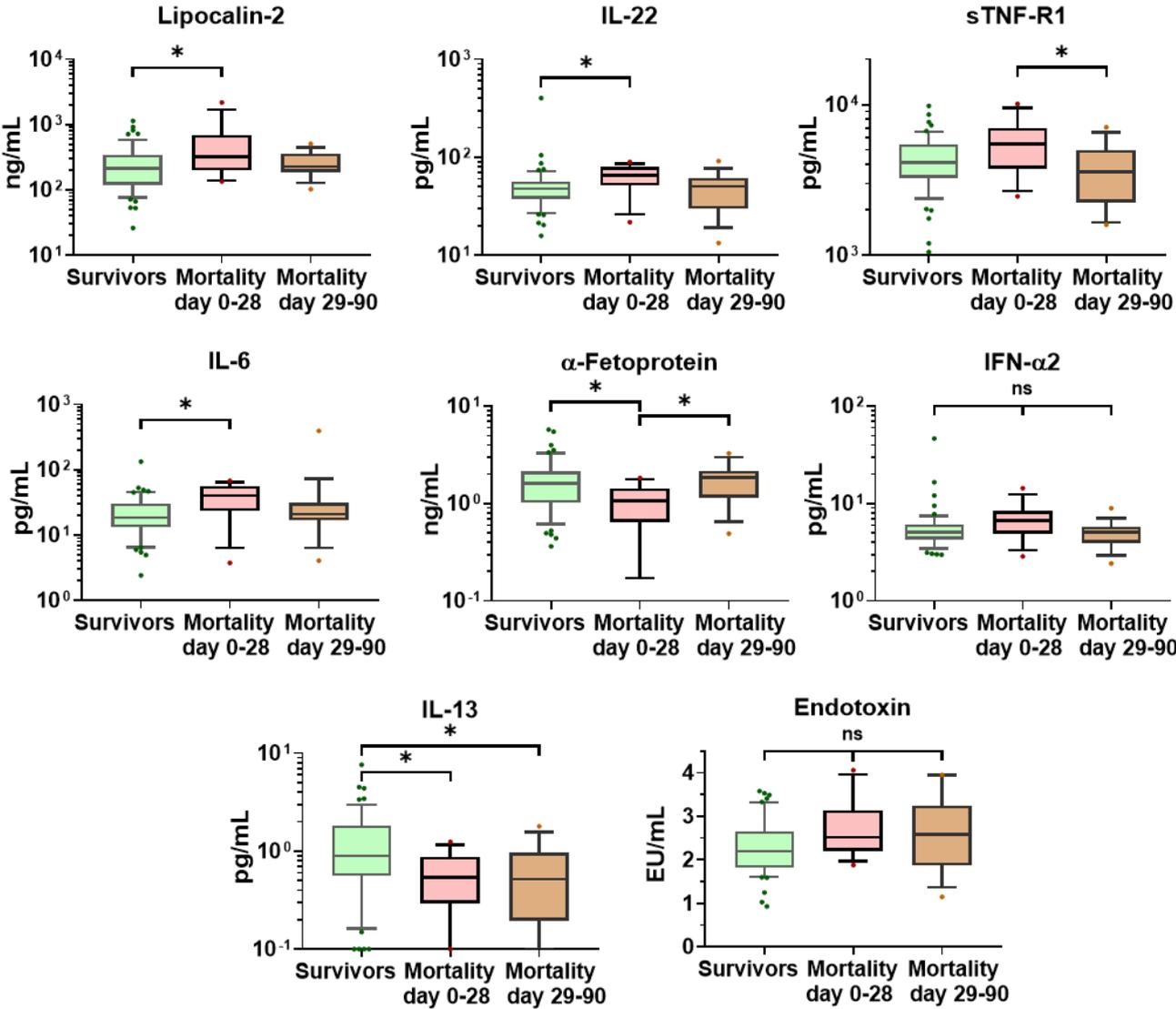
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Supplementary Figure 1



Flowchart showing the inclusion algorithm of AH patient and the availability of samples for the present study.

Supplementary Figure 2



Breaking down marker levels into survivors vs. early (1-28 day) vs. late (29-90) non-survivors reveals the reason of time-dependent association between markers and mortality. Markers associated with early mortality (Lipocalin-2, IFN-α2, sTNF-R1, α-fetoprotein, IL-22, IL-6) showed altered levels in patients who died within the first 28 days compared to both survivors and patients who died latter (between day 28-90). Markers associated with latter mortality had similar levels in non-survivor groups regardless of the time of death.

Supplementary Table 1

Markers showing altered levels between severe alcoholic hepatitis patient with and without cirrhosis.

	Patients without cirrhosis		Patients with cirrhosis		P value
	Median	IQR	Median	IQR	
Sonic Hedgehog	141.40	101.35-223.33	233.09	152.25-308.35	0.004
IFN-B	19.61	16.79-25.96	24.66	20.53-32.58	0.037
IL-20	18.88	17.38-20.72	24.90	20.84-29.94	0.001
MMP-2	153.04	126.12-195.74	233.53	179.90-307.31	0.001
Osteopontin	268.24	199.51-315.38	196.99	169.42-259.55	0.024
IL-1Ra	605.43	323.18-1699.24	250.80	160.53-703.46	0.022
LBP	40.44	29.03-47.75	26.80	18.50-34.53	0.003
IL-9	208.52	129.30-218.20	144.72	100.50-185.62	0.023

IL: interleukin; INF: interferon; LBP: lipopolysaccharide binding protein; MMP: metalloproteinase.

Supplementary Table 2

Univariable Cox regression analyses were for testing 28-day mortality predicting abilities of clinical factors, laboratory parameters and biomarkers (lipocalin-2, α -fetoprotein, IL-6, IFN- α 2, IL-22, sTNF-R1).

28-day Mortality	Univariable Cox regression analysis		
	HR	95.0% CI	p value
Treatment	0.648	0.212-1.981	0.447
Sex	0.244	0.054-1.101	0.067
Age	1.097	1.033-1.165	0.003
Cirrhosis	1.513	0.335-6.828	0.59
Previous AD	1.501	0.476-4.730	0.488
Ascites	1.946	0.654-5.790	0.232
Encephalopathy	5.988	1.952-18.367	0.002
AST (Ln)	0.591	0.172-2.034	0.405
ALT (Ln)	1.338	0.506-3.541	0.557
AST/ALT ratio	0.685	0.416-1.127	0.137
ALP (Ln)	0.28	0.074-1.062	0.061
INR (Ln)	9.326	0.865-100.584	0.066
Bilirubin (Ln)	2.239	0.517-9.696	0.281
Albumin	0.441	0.023-8.446	0.587
Creatinine (Ln)	2.626	0.969-7.113	0.058
WBC (Ln)	0.730	0.269-1.982	0.537
Lipocalin-2 (Ln)	2.708	1.305-5.619	0.007
α -Fetoprotein (Ln)	0.735	0.583-0.927	0.009
IL-6 (Ln)	1.793	1.007-3.192	0.047
IFN- α 2 (Ln)	2.167	0.905-5.188	0.082
IL-22 (Ln)	2.202	0.924-5.250	0.075
sTNF-R1 (Ln)	4.899	1.201-19.981	0.027

Laboratory parameters and biomarker levels were logarithmically transformed (Ln) before the analysis. Numbers in bold highlight significant predictors. AD: acute liver decompensation; ALP: Alkaline Phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; IL: interleukin; INR: international normalized ratio; INF: interferon; sTNF-R1: soluble tumor necrosis factor receptor; WBC: white blood cells.

Supplementary Table 3

Univariable Cox regression analyses for testing 90-day mortality predicting abilities of clinical factors, laboratory parameters and biomarkers (IL-6, IL-13).

90-day Mortality	Univariable Cox regression analysis		
	HR	95.0% CI	p value
Treatment	0.744	0.365-1.520	0.417
Sex	0.474	0.218-1.031	0.060
Age	1.067	1.027-1.110	0.001
Cirrhosis	1.407	0.537-3.689	0.487
Previous AD	0.856	0.377-1.944	0.710
Ascites	1.968	0.972-3.985	0.06
Encephalopathy	2.021	0.950-4.301	0.068
AST (Ln)	0.906	0.420-1.956	0.801
ALT (Ln)	1.554	0.807-2.993	0.187
AST/ALT ratio	0.786	0.591-1.045	0.097
ALP (Ln)	0.729	0.316-1.680	0.458
INR (Ln)	7.387	1.357-40.225	0.021
Bilirubin (Ln)	1.492	0.624-3.568	0.368
Albumin	0.316	0.050-1.984	0.219
Creatinine (Ln)	1.973	1.025-3.798	0.042
WBC (Ln)	1.181	0.613-2.277	0.619
IL-6 (Ln)	1.486	0.982-2.248	0.061
IL-13 (Ln)	0.754	0.617-0.922	0.006

Laboratory parameters and biomarker levels were logarithmically transformed (Ln) before the analysis. Numbers in bold highlight significant predictors. AD: acute liver decompensation; ALP: Alkaline Phosphatase; ALT: alanine transaminase; AST: aspartate transaminase; IL: interleukin; INR: international normalized ratio; INF: interferon; WBC: white blood cells.